

## TB and HIV A Biologic Synergy

What Nurses need to know about TB and HIV

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Why do we care?

In HIV-infected individuals, TB causes more deaths worldwide than any other condition

“What is global is local”

### Biologic Synergy between TB and HIV

- HIV makes TB worse:
  - Profound immunosuppression
  - Increases susceptibility to TB
  - Rapid progression from infection to disease
  - Difficult to diagnose due to reduced organisms in sputum
- TB makes HIV worse:
  - Immunologic stimulation accelerates progression
  - Increased replication of HIV at TB infection sites
  - HIV heterogeneity causes more difficult treatment

### TB and HIV in the US

- TB occurs mostly among immigrants
- Infrequently an AIDS-defining diagnosis
- Important to HIV clinicians because:
  - TB is so infectious
  - TB is curable with proper treatment
  - Improper treatment leads to drug resistance
- HIV is most important factor in progress to active TB
- Effective diagnosis and cure of TB reduces disease burden, reduces transmission and prevents resistance
- Effective ART is critical component of care

## LTBI

- HIV-infected persons with latent TB infection have a much higher risk of developing active TB
  - 10% lifetime risk in general population
  - 10% per year risk in HIV-co-infected population
- Identification and treatment is high priority
  - Reduces risk of disease to the individual
  - Reduces risk for further TB transmission
  - Progression to TB is reduced by HIV treatment, but never reaches zero, so there is always a risk

## Diagnosis of TB Infection is the Key

- TST –
  - PPD is preferred method due to utility of cost as well as utility for initial and annual testing
  - False negatives in persons with immunosuppression
- IGRA –
  - preferred for history of BCG exposure
  - high risk of failure to return for reading
- Anergy Testing – not recommended – no advantage

## Diagnosis of TB Infection is the Key

- Negative CXR – offer INH Treatment
  - 6-36 months
  - 9-months standard in US
- Abnormal CXR or Symptomatic – further assessment
- Low Suspicion – begin INH immediately
- High Suspicion – treat for active disease while cultures pending (4-months treatment)
- Significant exposure with negative test – LTBI Rx
- Previous TB or inadequate treatment – evaluate for active TB regardless of TST or IGRA results

## LTBI in Pregnancy

- Recommend standard prophylaxis of INH for 9-months with pyridoxine – even during first trimester
- Alternative agents (Rifampin or Rifabutin) should be used with caution and exposed neonates receive vitamin K to reduce risk of hemorrhagic disease
- May have trouble getting some pregnant women to agree to this but work with HIV case managers and OB physicians to promote the preferred treatment recommendations because of high risk of progression to active disease.

### Active MTB Disease

- Negative TST or IGRA can occur in up to 25% of HIV infected persons with active TB – does not rule out active disease
- Initiate respiratory precautions for HIV infected patients with undiagnosed chronic cough or inflammatory infiltrate on CXR until TB ruled out
- MTB usually causes pulmonary disease, but can also cause meningitis or disseminated disease
- Patients with lower CD4 counts more likely to manifest atypically in the chest

### Active MTB Disease

- Atypical CXR presentations include:
  - Absence of cavities
  - Presence of lower lobe disease
  - Hilar or mediastinal adenopathy
  - Miliary pattern presentation
  - Pleural effusions
  - Normal appearing CXR
- Differential diagnosis is extensive and depends on degree of immunosuppression

### Treatment Considerations

- Antiretroviral Therapy (ART) decreases mortality in HIV infected persons with active TB and should be initiated or optimized in everyone with TB and HIV co-infection.
- Risk of death is substantially lower if ART is initiated early – especially in patients with lower CD4 counts – indicative of severe immunosuppression.
- **In all cases, TB treatment should be started immediately upon diagnosis**

### Treatment Considerations

- Risk of paradoxical immune response – IRIS – in patients who start ART early
- Adherence to both treatments is the most important treatment issue once the diagnosis has been made
- Intermittent therapies should not be used
- Duration of treatment may be extended
  - Cavitory TB
  - Sputum remains positive after 2-months
  - Extra-pulmonary TB
  - Meningeal and Bone or Joint TB

## Treatment Considerations

- Drug – Drug Interactions
  - Rifampin interacts with many classes of HIV drugs
    - NNRTI's
    - Protease Inhibitors
    - Integrase Inhibitors and CCR5 antagonist
  - Rifampin does not adversely affect NRTI or FI classes
  - Safest combination with Rifampin is two-drug NRTI backbone with efavirenz
  - Rifabutin – fewer interactions, requires dosage changes
  - Already on ART – reassess total regimens
- If possible consider total pill burden

## Treatment Considerations

- Tables available from CDC website
- HIV literature recommends that patients with suspected TB (positive test or symptoms) be referred to the public health department – **so you will be seeing these patients**
  - Coordinate TB and HIV treatment regimens
  - Avoid or adjust for drug interactions
  - Assist in possible treatment confusion in the event of IRIS or exacerbation of other opportunistic diseases
  - Maximize adherence to medication regimens

## THE GOOD NEWS

- Drug-susceptible TB remains highly curable – even for persons with HIV infection
- There is demonstrated reduced mortality when ART is combined with TB chemotherapy

## Immune Reconstitution Inflammatory Syndrome - IRIS

- Small percentage (<25%) develop inflammatory disease in response to specific opportunistic pathogens (TB and others) within a few weeks of initiating antiretroviral therapy (ART)
  - Paradoxical
  - Unmasking
- Patients on treatment of active TB who begin ART may experience increase in symptoms of TB that is caused by enhanced immune response against the remaining MTB organisms – occurs secondary to immunologic improvement from ART

## Immune Reconstitution Inflammatory Syndrome - IRIS

- May occur at any point from 2-weeks to 1-year after ART is initiated, but average is 90 days
- Accompanied by sharp drop in HIV viral load and twofold increase in CD4 count
- Can sometimes occur during TB treatment alone
- Clinical presentation is nonspecific – no lab markers
- Usually occurs in patients:
  - With low CD4 counts (<50-100 cells/ml)
  - With elevated HIV viral load (>100,000 copies/ml)
  - When ART is initiated soon after TB treatment

## Immune Reconstitution Inflammatory Syndrome - IRIS

- First must rule out other causes of illness
  - TB (or other OI) treatment failure
  - HIV treatment failure
  - Presence of another Opportunistic Infection
  - Drug toxicities
- Red flags for IRIS diagnosis (vs. TB progression)
  - Absence of poor adherence or resistance
  - New or worsening fever or lymphadenopathy
  - New effusions
  - Non-pulmonary presentations – CNS, skin or visceral abscesses, bone lesions, hypercalcemia

## Immune Reconstitution Inflammatory Syndrome - IRIS

- Diagnosis of Exclusion – rule out all other causes
- Treatment should include
  - **Continue TB treatment – without question**
  - Continue ART – if possible
  - Treat other unmasked OI's if possible
  - Manage symptoms with NSAID's or steroids
- If a patient with TB-IRIS has already finished a full course of treatment for TB, repeat treatment is not indicated
- Co-infection with HIV and TB is epidemic in many countries - IRIS is not uncommon in patients with TB

## Remember This

- All persons with HIV infection should be routinely tested for TB
- All persons with a positive TB test should be routinely tested for HIV
- TB makes HIV worse
- HIV makes TB worse
- Begin TB or LTBI Rx immediately



### Remember This

- Optimally begin ART 2-8 weeks after initiation of TB treatment
- Watch for drug-drug interactions
- Watch for Immune Reconstitution Inflammatory Syndrome – IRIS
- Communication between TB and HIV clinicians is critical to success

### Remember This

### Nurses are the Key

To successful adherence with  
TB and HIV treatment

Hang in there with the patient and keep  
them on treatment

### Remember World AIDS Day

Thursday  
December 1, 2011



### Thank You

Questions? Contact me:

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